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PARTICLE STUDYING APPARATUS WITH SELF-CLEARING
SCANNER ELEMENT
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3,395,344

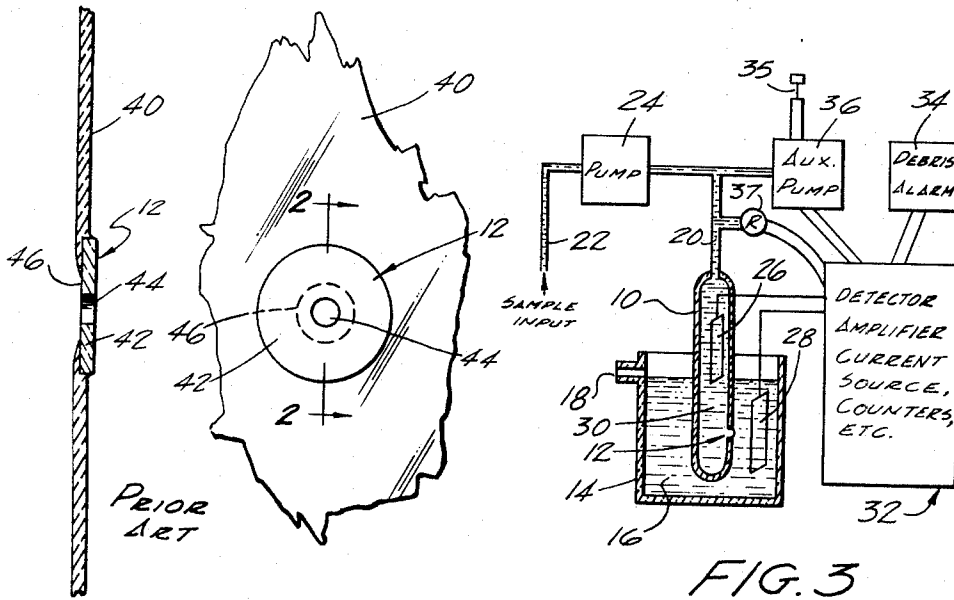


FIG. 2

FIG. 1

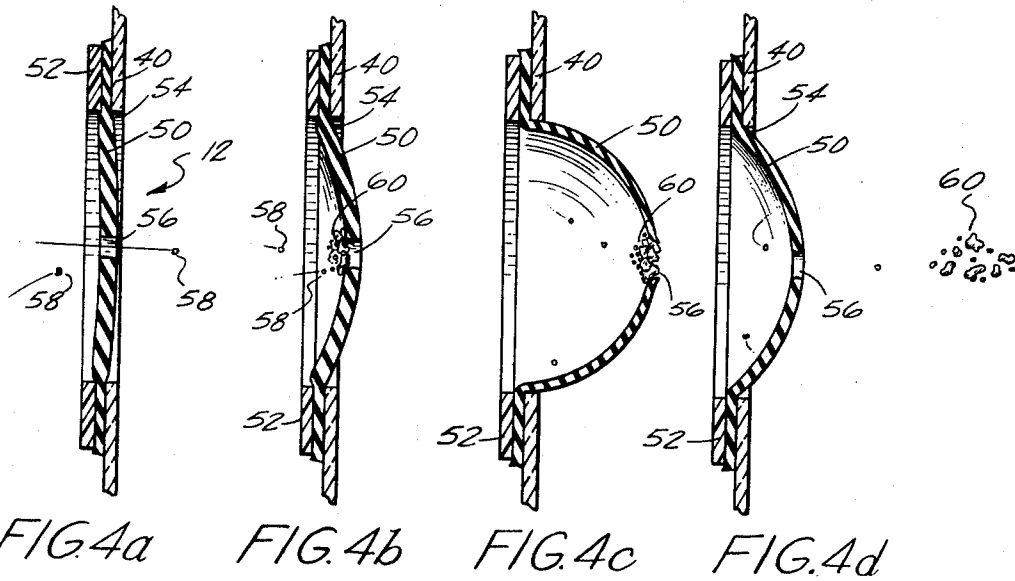


FIG. 4a

FIG. 4b

FIG. 4c

FIG. 4d

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PARTICLE STUDYING APPARATUS WITH SELF-CLEARING SCANNER ELEMENT

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ABSTRACT OF THE DISCLOSURE

Particle studying apparatus of the type wherein a suspension of particles in a fluid medium passes through a microscopic passageway from one fluid body contained in a first vessel to a second fluid body contained in a second vessel, said vessels electrically insulating their respective fluid bodies one from the other except through said microscopic passageway. The apparatus further including circuit means for establishing an electric path through said passageway such that upon connection of said circuit means to a power source and passage of particles through said passageway, detectable signals will be generated. A portion of said microscopic passageway being defined by a scanner element or the like which is provided with a microscopic aperture that determines the minimum cross-sectional area of said passageway, said scanner element being constructed of a flexible material such that under conditions occurring during blockage of the aperture by particles or pieces of debris present in said fluid medium said scanner element is adapted to expand to enlarge the aperture and alleviate blockage thereof.

This invention relates generally to particle counting and sizing apparatus of the Coulter type and more particularly is concerned with the construction of the particle scanning portion thereof.

The basic Coulter particle counting and sizing apparatus has become a standard device for accurately, quickly and reliably counting and sizing particles. The construction and operation of the structure is described in Coulter Patent 2,656,508. Scientific literature, texts and manuals set forth in considerable detail many ways of utilizing the apparatus. In view of this universal knowledge, the complete details of the apparatus need not be set forth. Suffice it for the purposes of this specification to note that the Coulter principle teaches that when a particle of microscopic or sub-microscopic size is passed through a microscopic aperture in a liquid whose conductivity is different than the conductivity of the particle, if at the same time a stable electrical current is being passed through the aperture, each time that a particle moves through the aperture there will be a detectable change in the resistivity of the effective volume of the aperture. This is readily detectable to produce an electrical signal which may be measured and counted.

The Coulter principle also teaches that the amplitude of the signal produced by the passage of a particle is proportional to the total mass of the particle, so that by suitable discriminating devices one may size particles for distribution studies.

Early in the history of the Coulter apparatus it became apparent that a serious problem connected with the device was clogging or plugging of the microscopic aperture which scanned the particles as they passed through. Some particle systems of wide ranges of particle size would be

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expected to have very large particles, even in minute quantities which can clog a microscopic aperture; other samples will have lint, dirt and other foreign matter; and still further in the study of biological particles by selective lysis, such as for example the counting and sizing of leukocytes after treatment of a blood sample with saponin, there will be considerable debris in a particle sample. These undesirable particles may be of sufficient size in and of themselves to cause clogging, or may coalesce to produce a clump which will hang in an aperture.

The effects of clogging an aperture can be loss of time, invalidation of a sample run, and the obtaining of inaccurate results of count and size.

Many methods have been suggested for the obviation of clogging, some of which are effective, and others of which are ineffective. Considerable expense can be added to the cost of a counting and sizing apparatus through the use of still others.

According to the invention, a very simple solution has been devised which is quite effective, and which involves little expense. An important object of the invention is to provide such a solution.

The aperture of the counting and sizing apparatus, which normally is in the form of a passageway in a rigid wafer or plate of glass or sapphire, is formed in accordance with the invention in a flexible and preferably elastic sheet. The sheet is secured in some suitable manner to an aperture tube.

Another object of the invention is achieved by the provision of such a sheet with aperture as the scanning element of the aperture tube, since such a scanning element is self-clearing.

Another object of the invention is to provide, in a particle counting and sizing apparatus of the Coulter type, a novel scanning element which is economical to manufacture and effective to clear itself, without substantial distortion or change in its dimensions.

Many other objects of the invention will occur to those skilled in this art as a description of the invention proceeds, in connection with which a preferred embodiment of the invention is illustrated and explained.

In the drawing:

FIG. 1 is a fragmentary plan view of an aperture tube of a Coulter counting and sizing apparatus, showing the known construction of scanning element, the scale being exaggerated, as are the scales of FIGS. 2 and 4.

FIG. 2 is a sectional view taken through the scanner element of FIG. 1 along the line 2-2 and in the indicated direction.

FIG. 3 is a diagrammatic view of a particle counting apparatus according to the invention, using the scanner element of invention.

FIGS. 4(a)-4(d) comprise a series of sectional views through a scanner element according to the invention, showing at a the element during use and in unclogged condition; at b the element after having become clogged by debris or the like; at c the element expanded, either by the pressure of the sample pump or by an auxiliary pump; and at d the debris having been expelled, the element returning to its normal condition.

The Coulter apparatus which is shown in FIG. 3 comprises an aperture tube 10 having its scanning element, shown generally at 12 immersed in a vessel 14 having a body of liquid 16 therein. The vessel 14 has an overflow spout at 18 in order to assure that the back pressure upon the scanning element is substantially regulated. The

aperture tube is connected to a conduit 20 whereby a sample suspension of particles may be introduced into the aperture tube 10 by way of the conduit 22 and a pump 24. Platinum electrodes 26 and 28 are immersed respectively in a body of suspension 30 within the aperture tube 10 and the body of liquid 16 in the vessel 14. The electrodes 26 and 28 enable the establishment of a stable electrical current between the two bodies through the aperture, and likewise enable the detection of the change in resistivity of the portion of the suspension effectively within the aperture. Leads as shown are connected to a block 32 which symbolically represents the electronic portion of the Coulter device, including detectors, pulse height analyzers, counters, the source of electric current for the aperture and other circuitry and apparatus.

It will be noted that there are connections from the block 32 to two other blocks 34 and 36, labelled respectively, debris alarm and auxiliary pump. The auxiliary pump 36 is connected to the conduit 20, for a purpose to be described.

It will be appreciated that the diagram of FIG. 3 is not intended to be a flow diagram or electrical circuit diagram, but merely an extremely simplified indication of the environment in which the invention finds application, and a sketch to assist in the explanation of the invention. For example, the apparatus shown is a continuous flow device, but could as well be a batch device, much like that shown in Coulter et al. Patent 2,869,078. Similarly the flow of suspension through the aperture of the scanning element 12 could be in the direction opposite to that shown or the pump 24 could be a source of vacuum. There could be other combinations of valving systems, metering apparatus, manometers, etc.

The most familiar type of scanning element is shown in FIGS. 1 and 2. The figures are marked "Prior Art" because the invention herein comprises a substantial improvement over the so-called rigid scanning element heretofore known. It is not intended by this comparison to derogate the position occupied by the glass or sapphire wafer in the art, since there have been countless studies and researches conducted with the rigid element. It is in universal use at this time. The improvement herein relates to self-clearing elements, to overcome, at least partially, a disadvantage which plagues many workers.

The aperture tube wall, designated in FIGS. 1, 2 and 4 by the reference character 40, normally is made of glass, plastic or some similar insulating material. The prior art element 12 consisted of a glass or sapphire wafer 42 having a central aperture 44 forming a passageway through the wall 40. The aperture 44 is the only physical and electrical passageway or path between bodies of fluid separated by the wall. The wafer 42 is cemented to a surface of the wall 40, or may be fused or otherwise physically attached. The wall 40 normally is prepared by forming a hole or orifice therein, as shown at 46, which is larger than the aperture 44 and smaller than the outer diameter of the wafer 42.

The construction of a scanner element and method of making the same using a sapphire wafer are described in U.S. Patents 2,985,830 and 3,122,431. Other methods are feasible.

The clogging of the aperture 44 by debris is undesirable because the time involved in clearing the same is lost. Further, the discovery of the clogging may be after improper results have been recorded as to count and sizing; giving rise to serious errors, etc. Normally a microscope is trained upon the aperture at all times, in order to watch for the signs of clogging. The chances of clogging occurring are dependent upon the size of the aperture, the size and type of particles being studied, the dilution of the particles, the chemistry of the particulate material, etc. In the case of blood cells, the aperture 44 is 100 microns in diameter, and this is quite small. The preferred aperture size normally is no larger than 3 to 50 times the average diameter of the particles being studied, for maximum sensitivity. Furthermore, the calibrated relationship

between the responses to different size particles depends upon the diameter of the aperture remaining constant throughout the determinations being made. Calibration over a period of time will depend upon maintaining the diameter of the aperture over that period.

Mechanical methods have been devised for clearing the debris from an aperture once discovered, including the crude method of wiping one's finger over the exposed face of the scanning element where one could reach it. This, of course, contaminates suspensions which may not be able to withstand such—or is dangerous if the suspension is corrosive. Likewise, electronic methods have been devised which depend upon the electrical change in the signal produced in case of clogging. Such signal change detection systems can be used to operate a debris alarm as shown at 34, cut off the counting, operate a mechanical clearing device, and so forth. In the invention, as will be seen, such a circuit can be used to operate an auxiliary pump 36 to apply an internal pressure to the fluid system to cause the scanner element to empty itself.

In FIGS. 4(a)–4(d) the scanner element 12 of the invention is illustrated in four different conditions. The element comprises a diaphragm 50 of flexible sheet material secured to a surface of the wall 40 by means of a retainer ring 52. The diaphragm 50 may be a small disc or a part of a larger envelope or sheet, held in place over a hole 54 provided in the wall 40. The ring 52 is annular in configuration, and although shown as plastic or glass, it may even be of metal. It may even be the inner electrode 26. It can be held in place by cement, clamping means (not shown) or in any other manner. Preferably, the diaphragm is under tension, so that it does not vibrate or distort to any substantial extent under the ordinary pressure exerted during a count. To accomplish this, it would be presecured to the ring 52 before mounting. It is appreciated that if the flow of suspension is from left to right, as intended in FIGS. 4(a)–4(d) and as described in connection with FIG. 3, then the installation of the scanner element 12 might pose some serious mechanical manipulation problems, but it should be pointed out that the diagrams are merely explanatory, and not intended to be limiting. The apparatus may take a form of completely different configuration, and use radically different glassware, such that trying to mount the element 12 to the inside of a tube will not be necessary.

A fine aperture 56 is formed in the center of the diaphragm 50 by any suitable means to provide the passageway for the particles, some of which are shown at 58. These particles 58 freely pass through the aperture 56 as shown in FIG. 4a because they are much smaller than the aperture, and because for the most part there is no coalescing or clumping of them. Note that the diaphragm 50 will belly slightly outward to the right because of the liquid pressure caused by the pump 24 which forces the suspension to move. The thickness of the diaphragm is shown to be of the order of the aperture diameter. There are very fine, flexible and elastic sheetings available commercially. These may be made thinner by stretching them over a securing ring such as 52.

In FIG. 4b, a clump of debris, as shown at 60, has clogged the aperture 56 and the particles 58 can no longer get through. If they do, the signals caused by the passage of particles will have much greater amplitude than they normally would since the aperture 56 is restricted and its sensitivity thereby will be increased. The flow of liquid decreases and if the pump 24 continues to operate, the pressure in the closed fluid system within the aperture tube 10 and conduit 20 rises and causes the diaphragm to expand as shown in FIG. 4b. This will decrease the thickness of the diaphragm, and increase the size of the aperture 56. The pressure increases and in FIG. 4c it will be noted that the diaphragm has stretched still further and belled out quite substantially. The aperture 56 is now quite larger.

Finally, as shown in FIG. 4d, the clump 60 has been ejected through the aperture 56, and with relief of

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pressure, the diaphragm returns to the condition of FIG. 4a, in which the aperture 56 is exactly as it was before the blockage.

Now, it has been assumed that there was a complete blockage for the purpose of explaining the manner of operation of the apparatus. The scanner element 12 of the invention may not respond precisely as described in all cases. It may belly without ejecting the debris clump 60, or the blockage may be caused by lint or fibres not completely stopping flow. Under such circumstances, the electronics may be arranged to detect this blockage or partial blockage, and apply a sudden burst of pressure to the system by the auxiliary pump 36 causing the ejection of the clump or lint. The pressure burst may be negative, as caused by applying a sudden vacuum to the conduit 20, thereby causing the diaphragm 50 to be sucked inward, stretched and relieved of its blocking material.

The material from which the diaphragm 50 is made is preferably elastic. Rubber sheeting is considered excellent, either in natural or synthetic form. Various resinous films of the "cellophane" type have been used, as well as the more flexible type, but these have been found not as advantageous for several reasons. In the first place they do not stretch as much as needed to assure discharge of the blocking materials, and in the second place, if they do stretch, they have a tendency to set and not return fully to original conditions. This means that the aperture 56 is enlarged, the sensitivity decreased, and the calibration changed. Such films will operate, but must be handled carefully, especially when high pressures are applied, in order to prevent rupture. Pressures must be limited to those which will not cause rupture.

The debris 60 may not occur at once but may result in accumulation, so that detection of the blockage should be made as seen as possible. The debris alarm 34 provides this, and in an application filed by Wallace H. Coulter and Walter R. Hogg, May 1, 1964, Ser. No. 364,070, several forms of electronically operating debris alarms suitable for such use are described.

In applying the so-called burst of pressure, one could use a manually operated positive displacement pump to change the pressure in the system. A manual pump handle is shown at 35. This might be done when one discovers the blockage, partial or complete, as a result of visual observation through the microscope or by other means, such as the debris alarm. One might perform this application of pressure manually, or mechanically, as a routine matter before each count to be certain that the aperture is clear. A pressure regulator 37 may operate pump 36 through electrical connection with the apparatus 32.

An additional advantageous arrangement in a system of this type is to cut off the operation of the data taking system until the apparatus has been restored to normal.

With respect to the manufacture of the diaphragms 50, these may be molded or may be formed of sheeting suitably perforated. In the construction of diaphragms of cellulosic material, which is flexible but not elastic, a heated stylus was used to punch the aperture. In the case of thin rubber sheeting diaphragms, fine hypodermic tubing was made into a punch and used for perforating the hole. Other methods will suggest themselves.

As used in the claims, the word "flexible" has the definition pliable in any manner, including elasticity, hence the word "flexible" is intended to have much broader meaning than the word "elastic." As to the definition of the word elastic, what is intended is the ability of the material to stretch to a size or shape having greater dimensions than in unstretched condition, and to return to its substantially original condition.

It is believed that the invention has been sufficiently described in order to enable those skilled in the art to understand and practice the same, without further description. Obviously there will be considerable room for variation

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without in any way departing from the spirit or scope of the invention as defined in the appended claims.

What it is desired to secure by Letters Patent of the United States is:

1. In an electronic particle study device of the type wherein a suspension of particles is analyzed and which includes, a pair of vessels with a microscopic passageway providing a path of communication between the interiors of said vessels, each vessel adapted to have a portion of said suspension contained therein with said portions insulated electrically one from the other except through said microscopic passageway, and circuit means for establishing an electric path through said passageway such that, upon connection of said circuit means to a power source and passage of particles through said passageway signals may be generated; the improvement wherein a portion of said passageway is defined by a scanner element comprised of a flexible diaphragm, said diaphragm having a microscopic aperture formed therein and constructed of a material such that under conditions occurring during blockage of said aperture by particles or the like, said diaphragm will distort to enlarge the aperture and alleviate blockage thereof.

2. An element as claimed in claim 1 in which the flexible diaphragm is formed of an elastic material and the distortion comprises expansion and increase of the diameter of the passageway.

3. An element as claimed in claim 2 in which the flexible diaphragm is formed of a rubber material.

4. In an electronic particle study device of the type wherein a suspension of particles is analyzed and which includes, a pair of vessels with a microscopic passageway providing a path of communication between the interiors of said vessels, each vessel adapted to have a portion of said suspension contained therein with said portions insulated electrically one from the other except through said microscopic passageway, and circuit means for establishing an electric path through said passageway such that upon connection of said circuit means to a power source and passage of particles through said passageway signals may be generated; the improvement wherein said device is provided with means to alleviate the blockage of said passageway by particles or pieces of debris present in said suspension, said means including an element associated with said vessels and having a microscopic aperture formed therein which defines the minimum cross-sectional area of said microscopic passageway, said element being constructed of a flexible material such that under conditions occurring during blockage of said microscopic aperture, said element will expand to enlarge said aperture and alleviate the blockage thereof.

5. Apparatus as claimed in claim 4 in which the material is elastic in addition to being flexible.

6. A device as defined in claim 4 wherein said means further includes pump means for maintaining a pressure differential between the respective portions of the suspension at a level such that the particles may be caused to pass through the aperture without substantially changing the dimensions thereof and for changing the level of said pressure differential to expand said element in the event the debris becomes lodged in the aperture.

7. A device as defined in claim 6 wherein said pump means comprises a pair of pumps, one of which is used only to change the pressure level when debris lodges in said aperture and blockage occurs.

8. A device as defined in claim 7 further including means for detecting blockage of the aperture and automatically operating the pressure level changing pump.

9. A device as defined in claim 4 further including apparatus to provide and record data related to the passage of said particles and the signals so produced, said apparatus including means to automatically discontinue the recording of data when said aperture becomes at least partially blocked.

10. A device as claimed in claim 7 in which the pres-

sure level change pump is operated by a change of pressure caused by clogging.

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